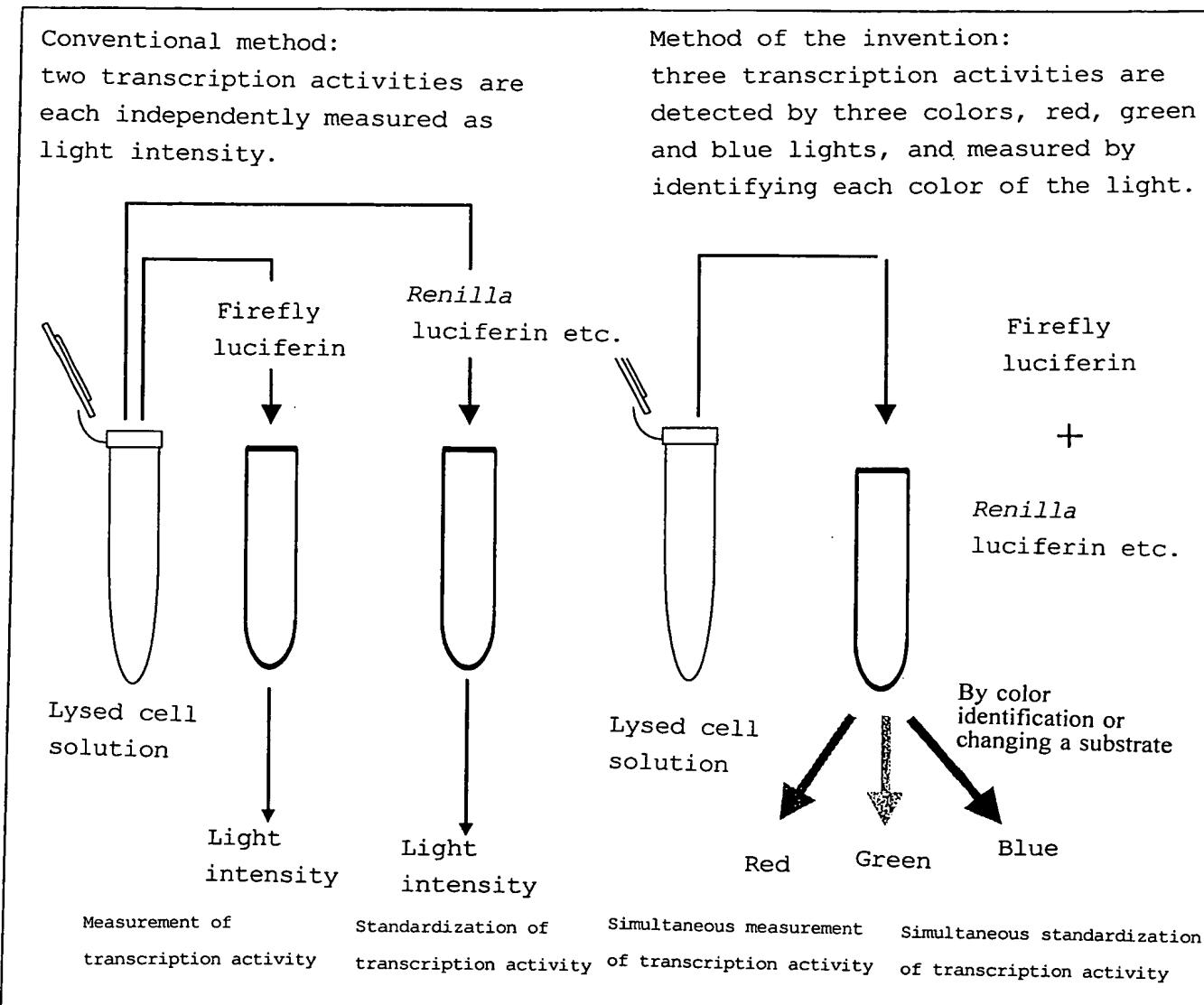
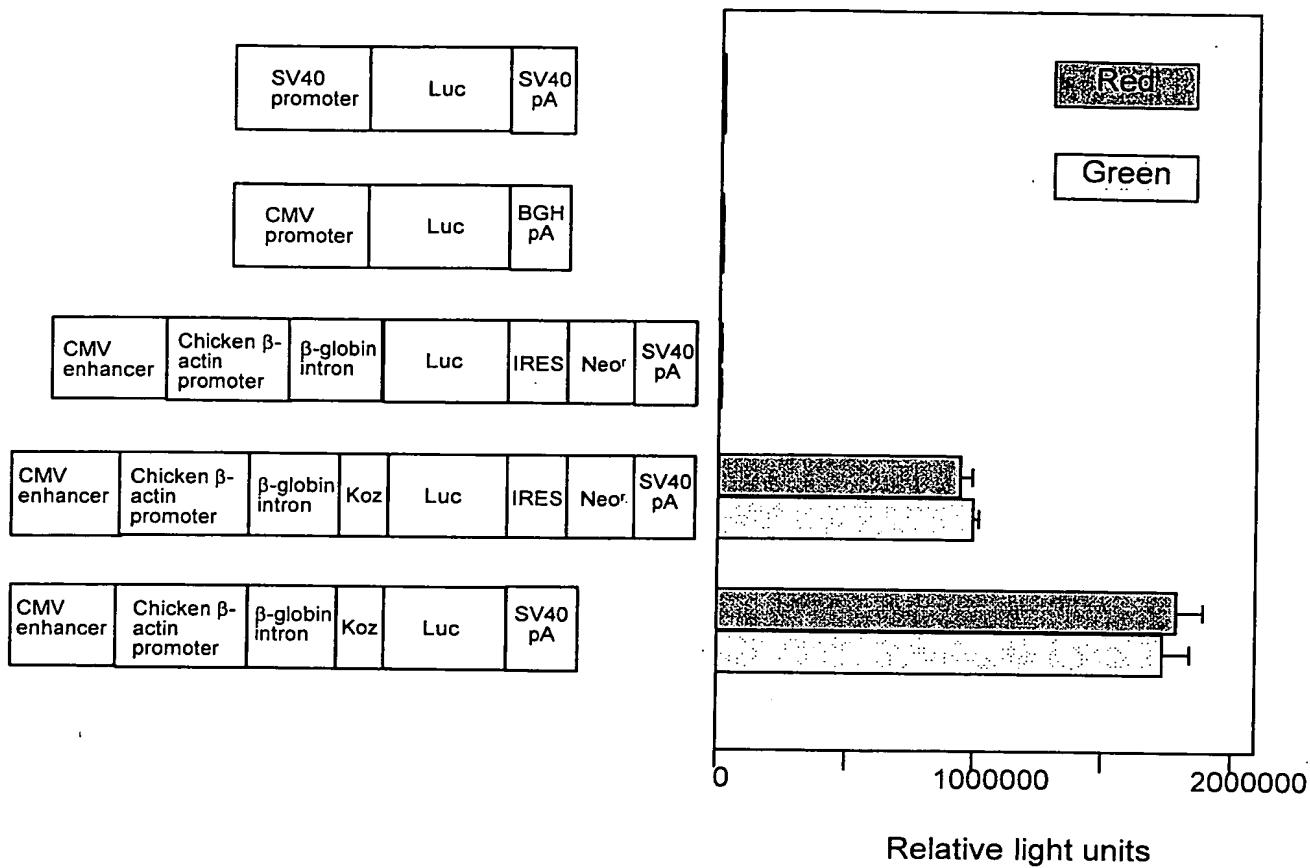
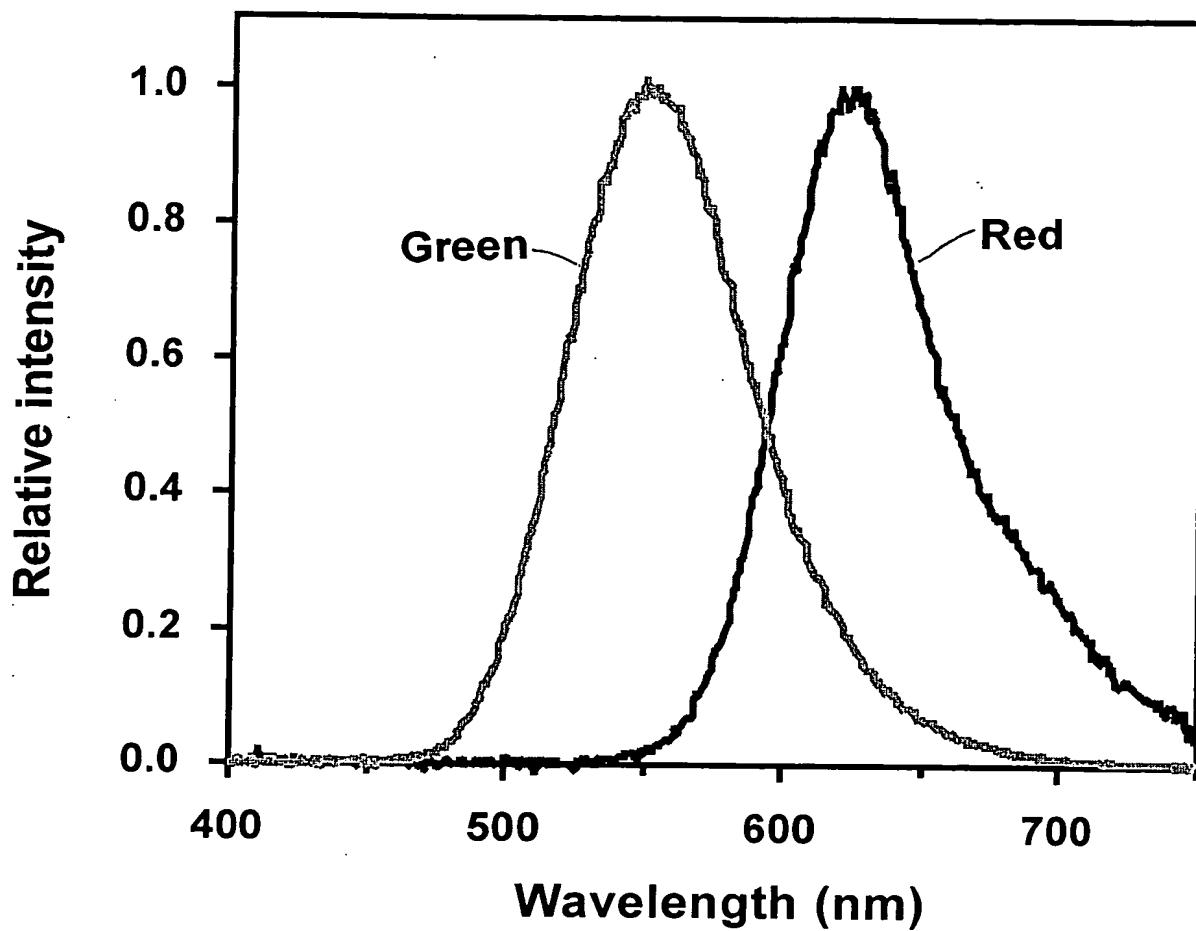


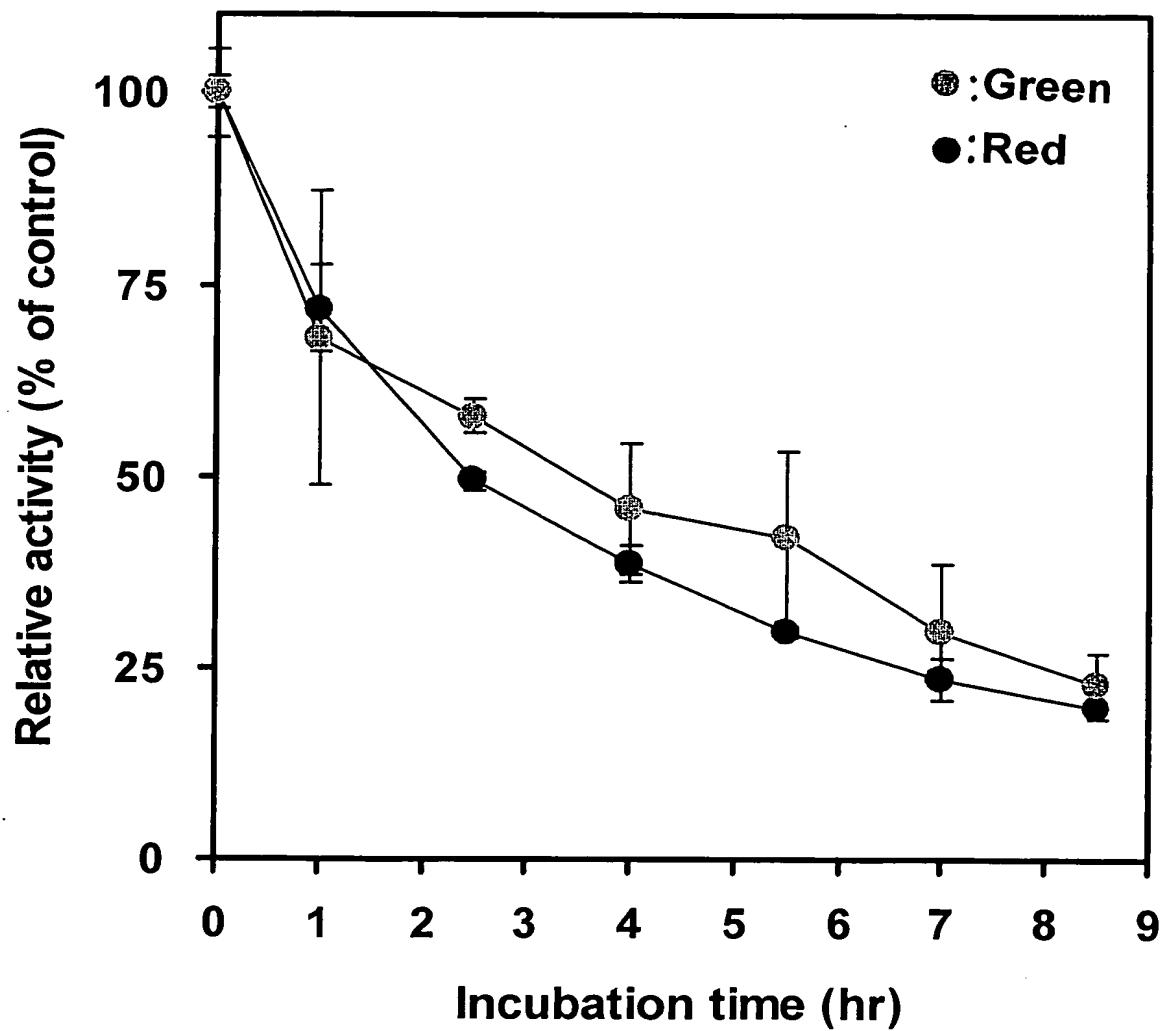
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Fig. 1



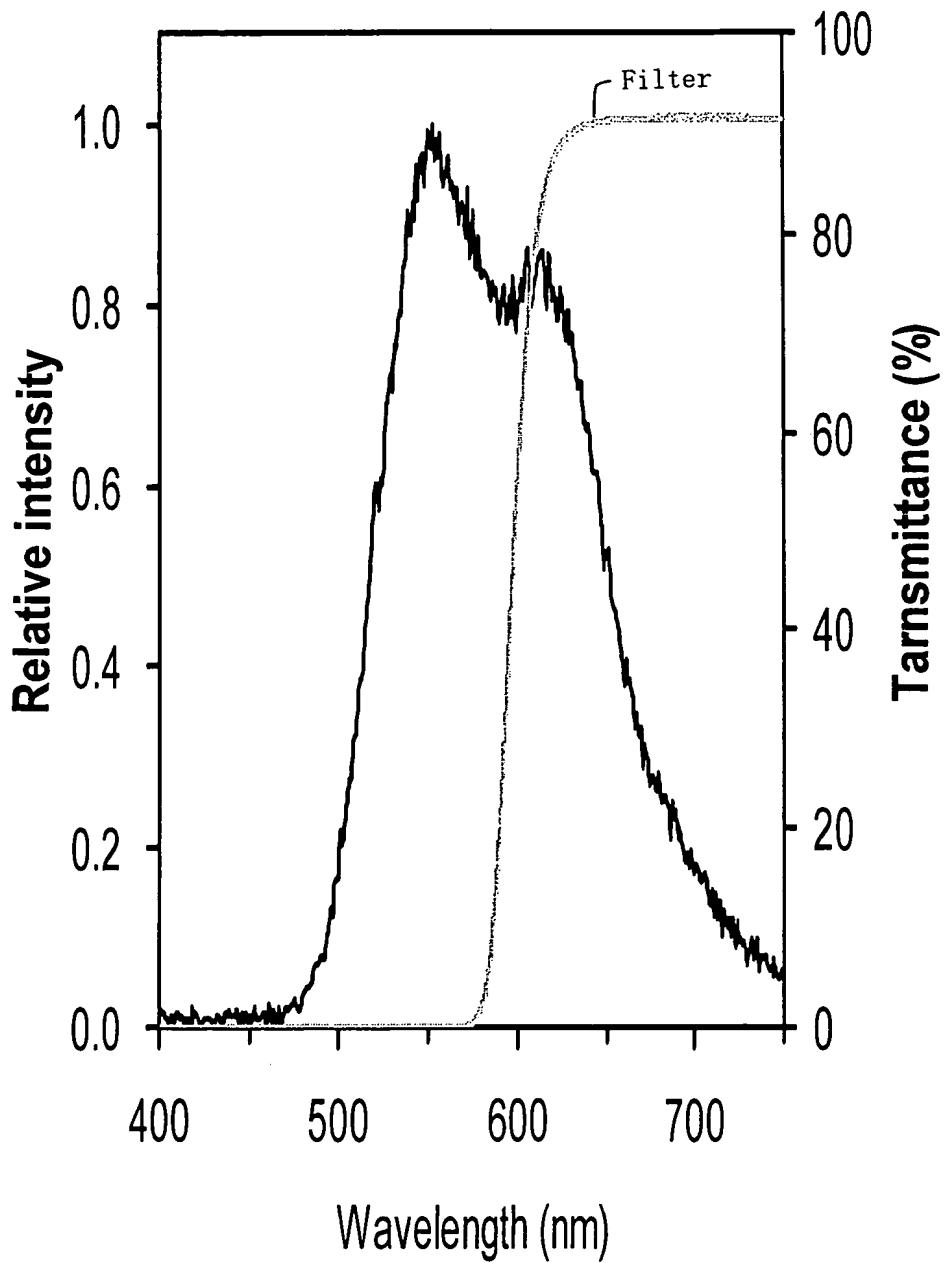
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Fig. 2

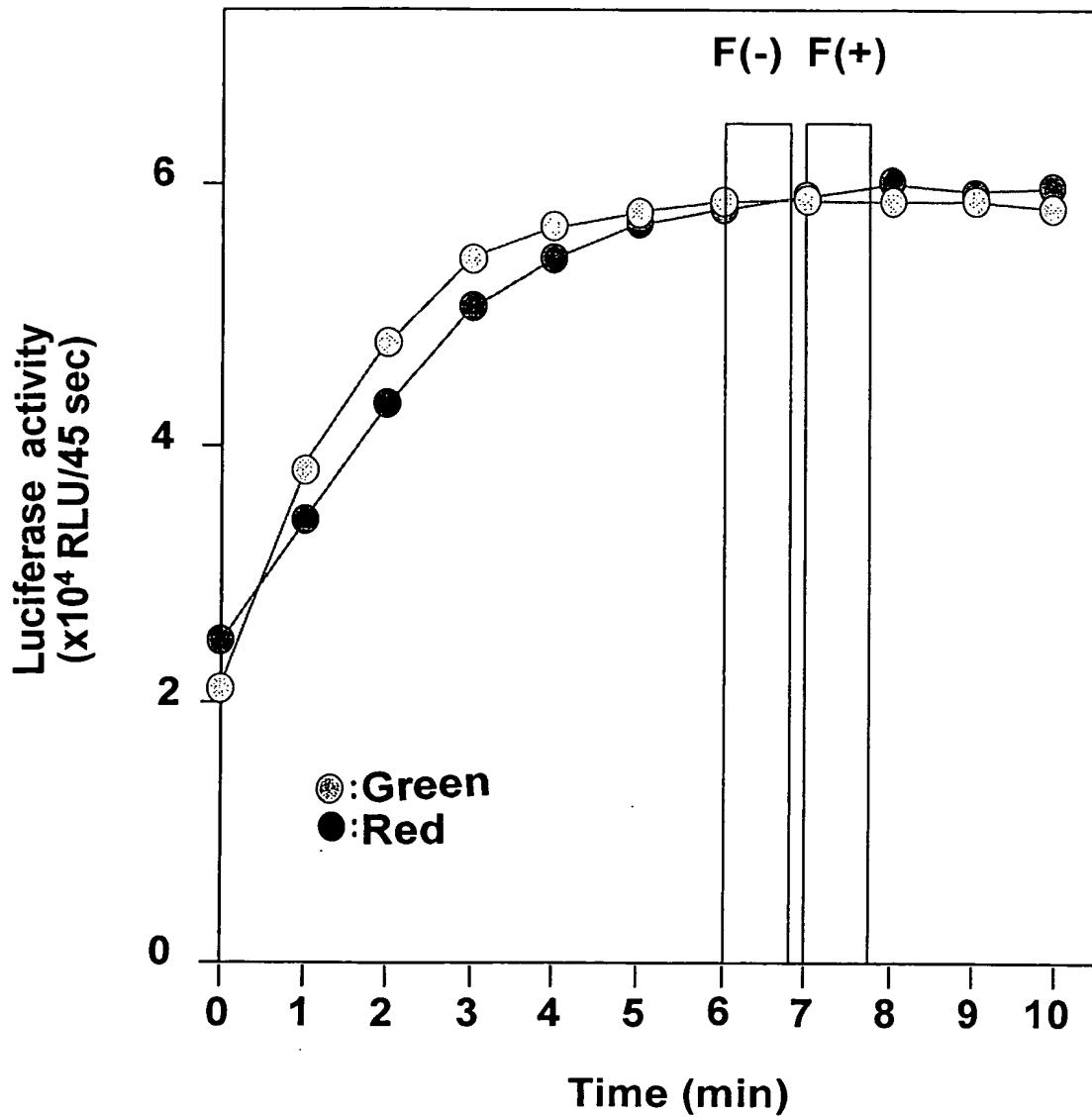
3 / 2 2
Fig. 3

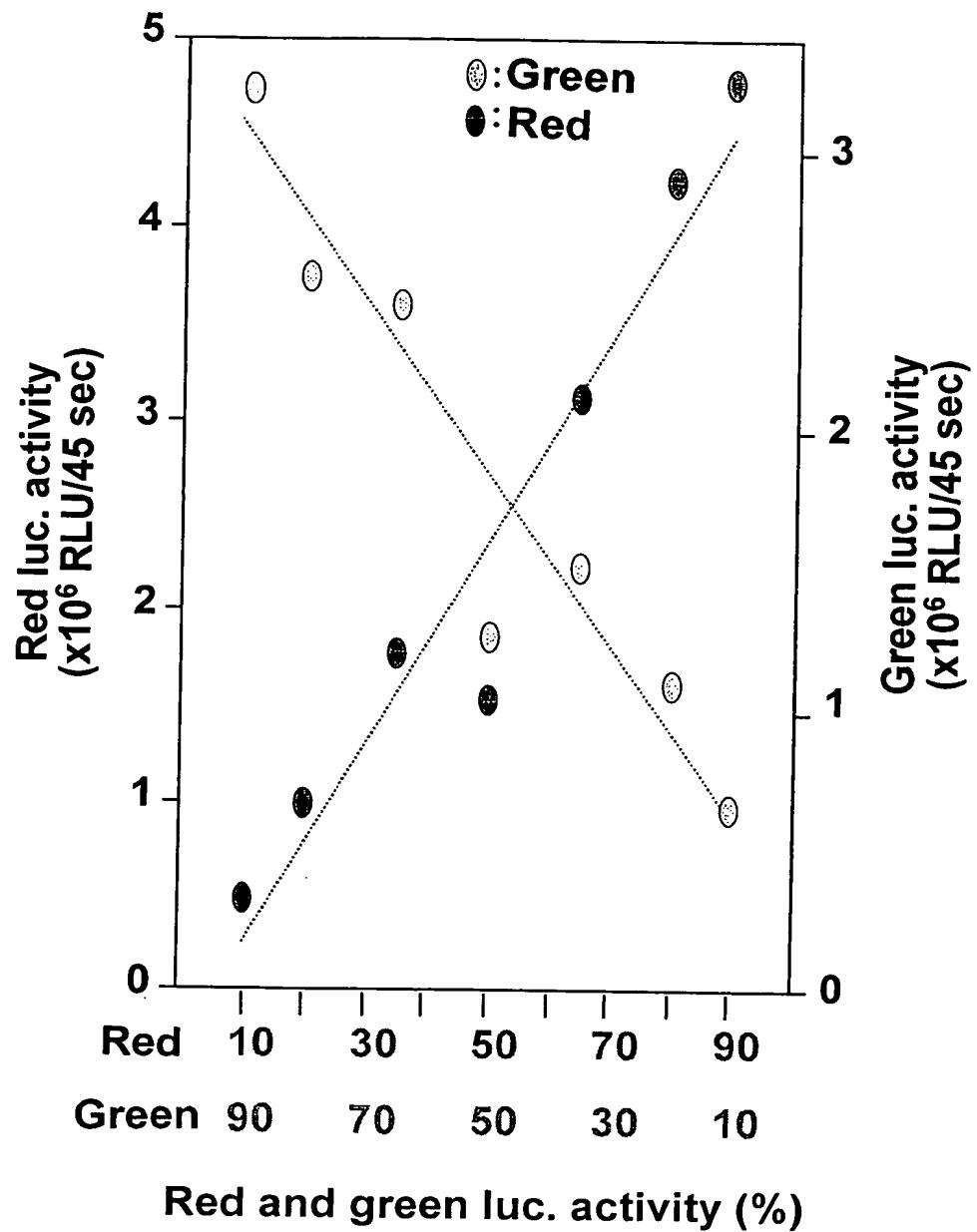
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Fig. 4

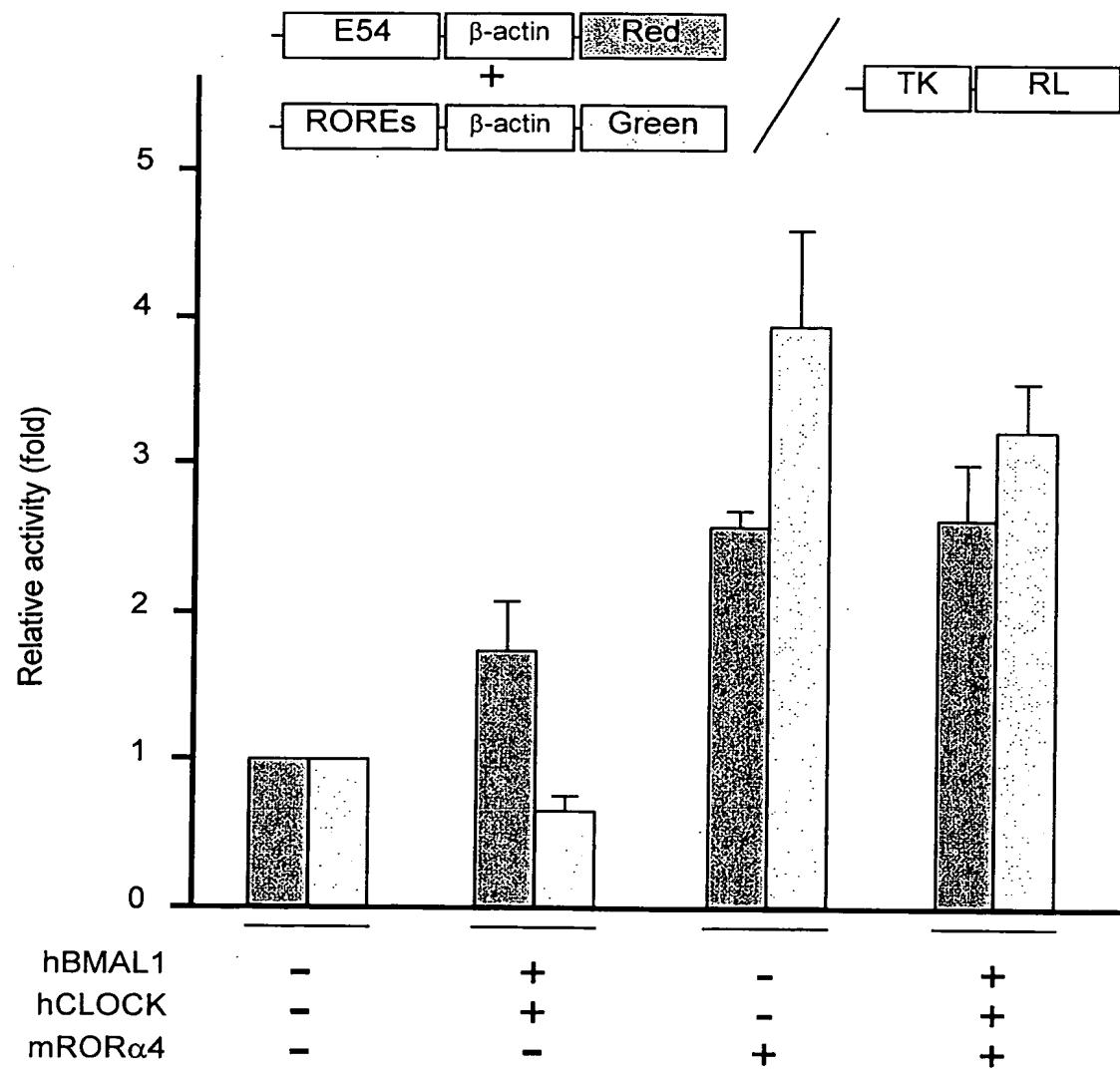
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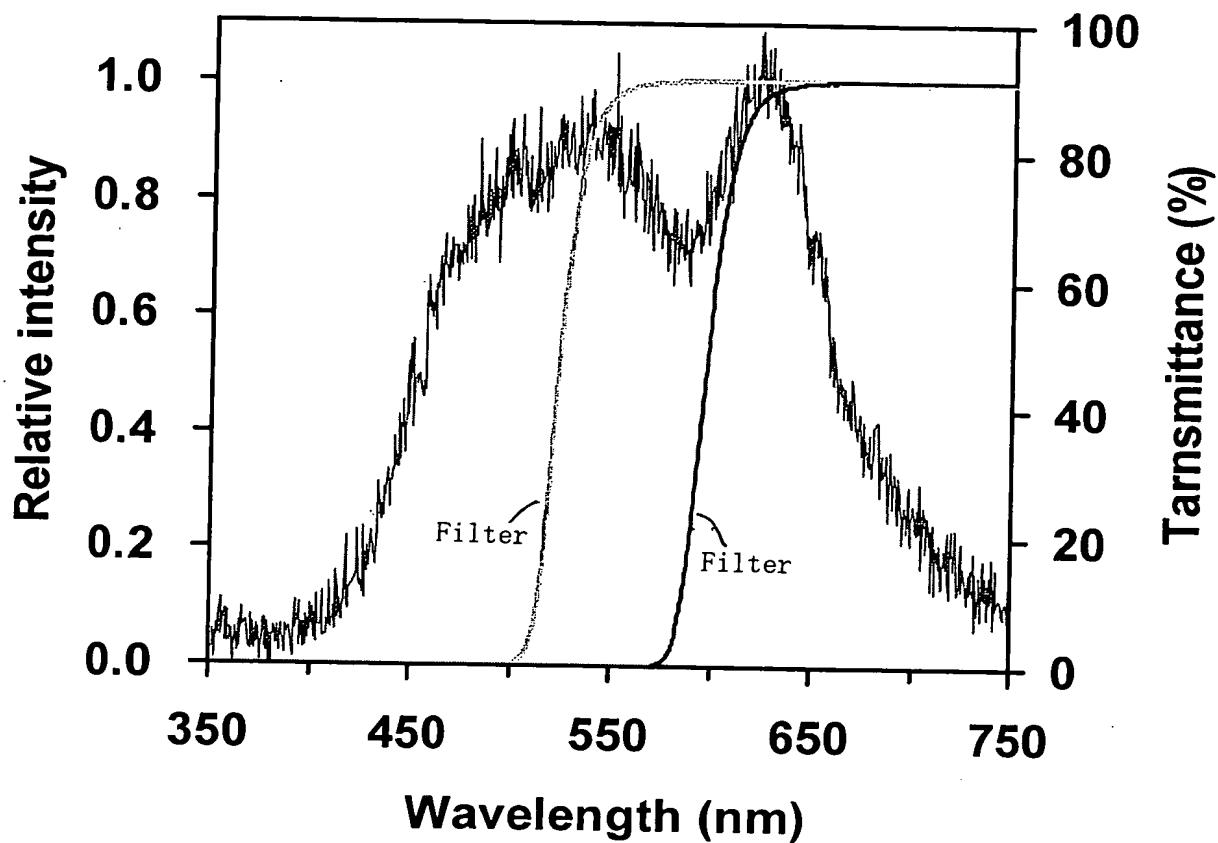
5/22
Fig. 5

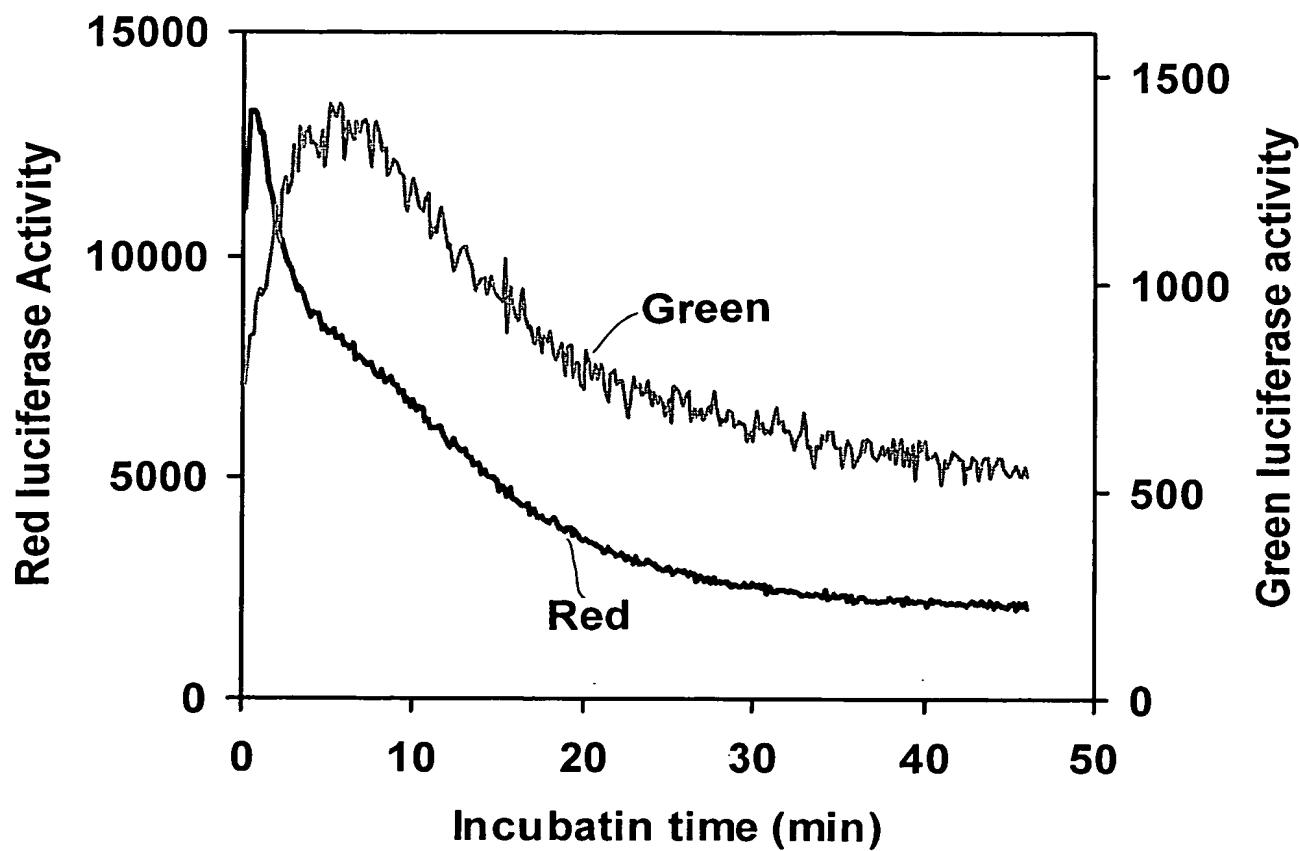


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Fig. 6

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Fig. 7

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Fig. 8

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Fig. 9

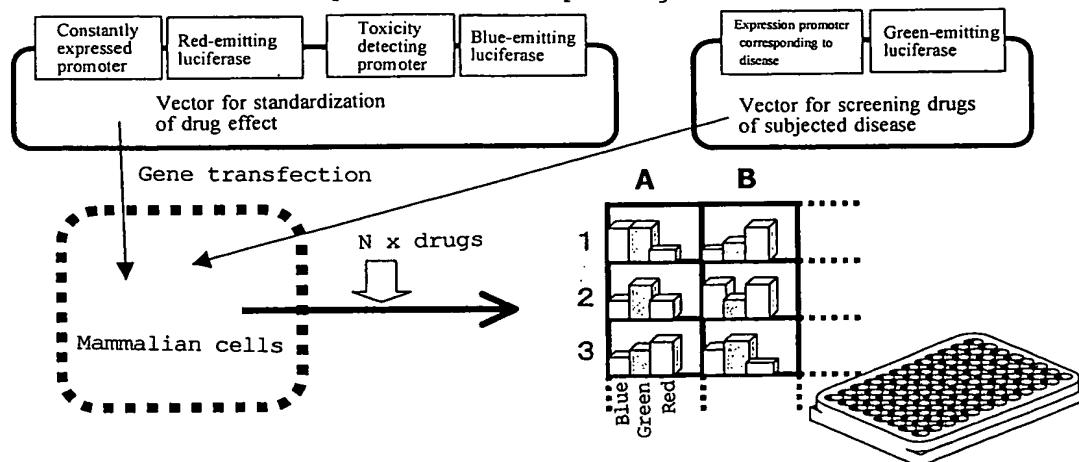
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Fig. 10

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Fig. 11

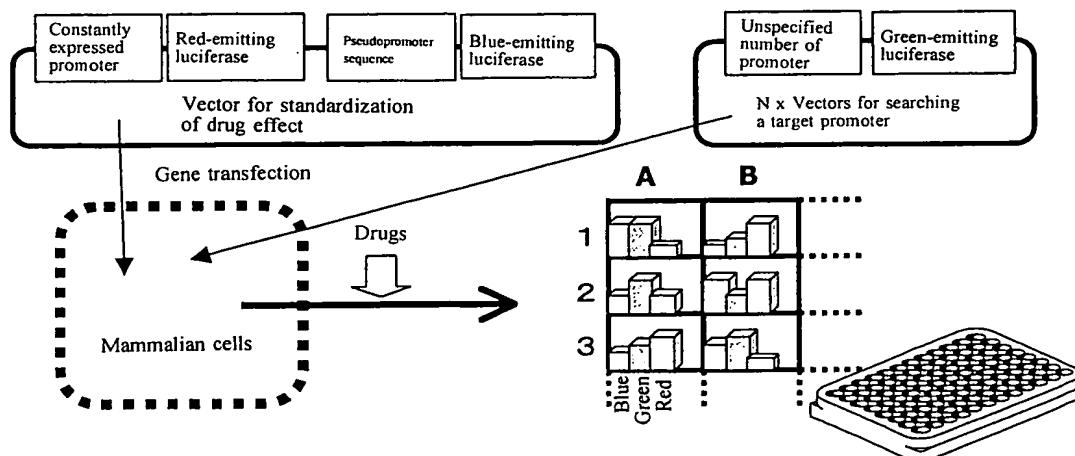
Many specimens are exhaustively analyzed in a primary screening.

Example 1: Screening for drugs which induce a gene expression corresponding to a disease



For example, in this primary screening, the red-emitting luciferase is a control, the blue-emitting luciferase detects the toxicity, and the green-emitting luciferase detects the drug effect. Therefore, it can be evaluated that the drug in an A1 column has the effect for the disease but works lethally and the drug in an A2 column has the similar effect to the A1 and is safer than the A1.

Example 2: Screening for gene expression regions which a certain drug affects

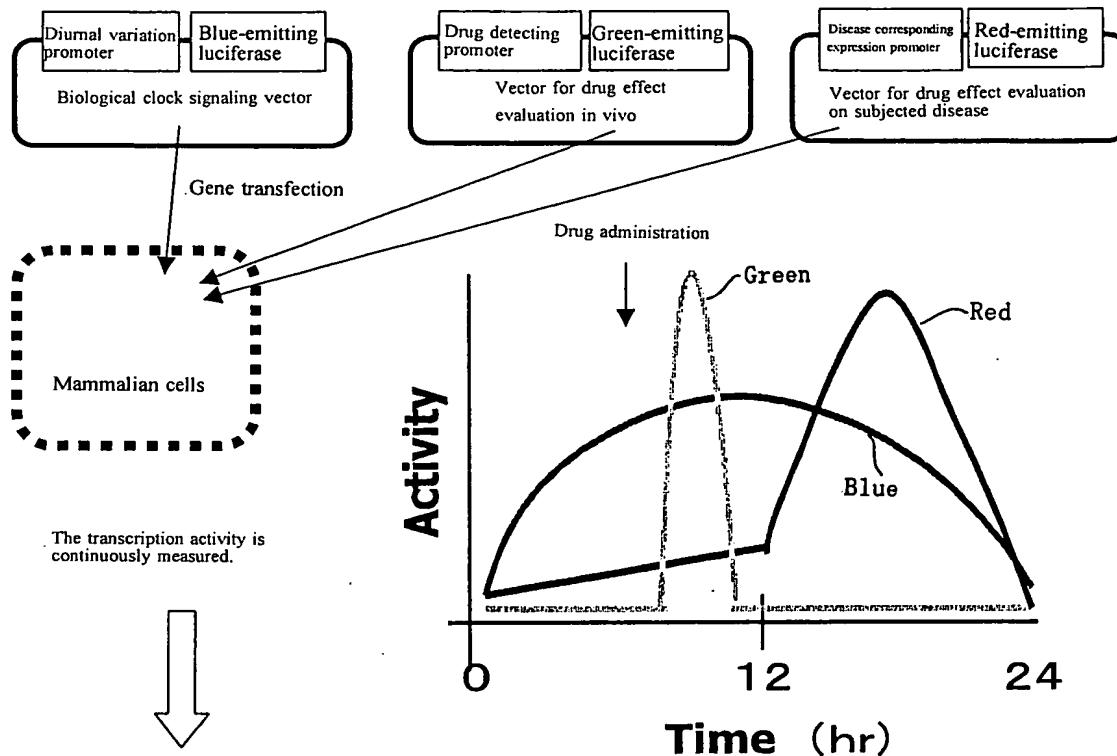


For example, in this primary screening, the red-emitting luciferase is a control, a pseudopromoter sequence is inserted in the blue-emitting luciferase, and the green-emitting luciferase reports a promoter with unknown function obtained from a promoter sequence library and evaluates a non-specific effect. A target site of the drug whose promoter target is not determined is screened. Therefore, for a certain drug, the promoter selected in an A1 column has the effect at first glance but is likely to be non-specific when determined by the blue, whereas the promoter in an A2 column has the same effect as that in the A1 column and is not non-specific so long as determined by the blue.

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Fig. 12

In the secondary screening, an individual event is evaluated.

Example: Drug discovery based on diurnal variation of body



For example, in the secondary screening, it can be evaluated whether the drug having an effect on the subjected disease works effectively for a patient or when the drug is administered is important. The blue-emitting luciferase is a promoter representing a diurnal change of a human biological clock and its maximum corresponds to daytime 12 hours. The green-emitting luciferase and the red-emitting luciferase suppose a transient effect of the drug and a promoter region where the drug works finally, respectively. It is found that when the drug is administered at 6 o'clock in the morning shown by the blue, the green which represents the effect on the drug transiently increased after one hour due to a shock thereof, but the effect thereof disappears in several hours, the effect of the drug is gradually increased around a noon. From this result, the drug discovery which makes a design of an administration time, the influence and effect of the drug suitable becomes possible.

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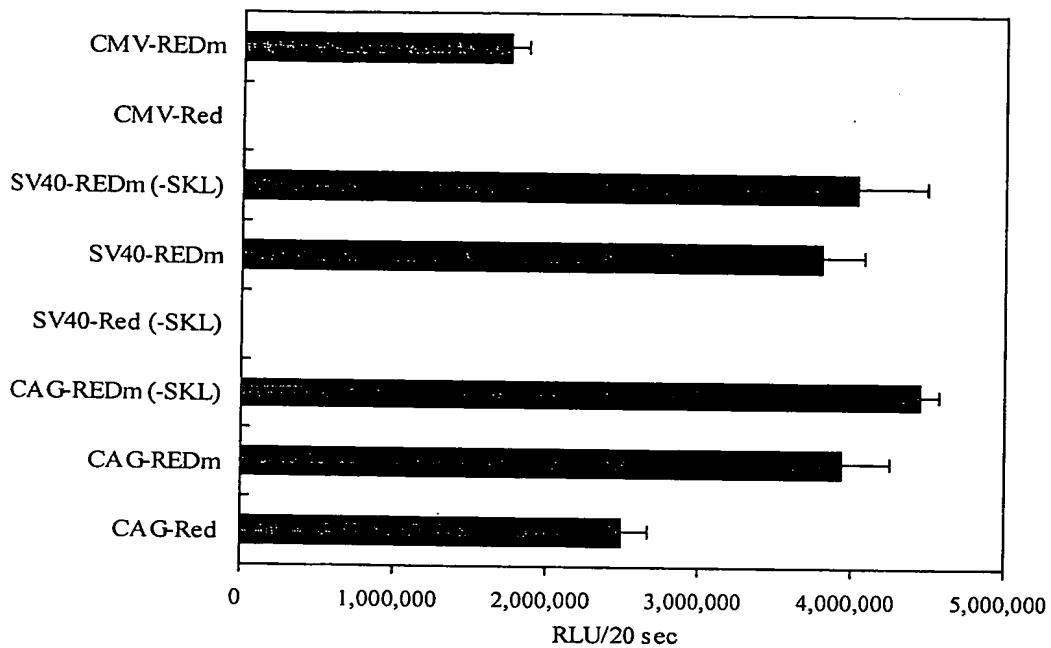
Fig. 13

RedWT	1	ATGGAAGAAGA	AAACAT	CTGAATGG	GATCC	CTCG	GATCT	CTT	CTGGCACA	60	
REDm	1	ATGGAAGAAGA	AAACAT	CTGAATGG	GATCC	CTCG	GATCT	CTT	CTGGCACA	60	
RedWT	61	GC	GG	CT	TA	TT	AT	TC	AT	AC	60
REDm	61	GC	GG	CT	TC	AG	GT	CT	TC	GG	60
RedWT	121	GAT	GCC	CA	AC	CA	TA	TC	AT	AC	120
REDm	121	GAT	GCC	CA	AC	CA	CG	GT	CT	GG	120
RedWT	181	GC	AT	TC	AG	TA	TC	AT	TC	AA	180
REDm	181	GC	AT	TC	AG	TA	TC	AT	TC	AA	180
RedWT	241	ACAA	ACAT	CT	TT	GG	CT	TT	GG	CT	240
REDm	241	ACAA	ACAT	CT	TT	GG	CT	TT	GG	CT	240
RedWT	301	AC	AT	AA	AT	GT	AC	CA	AG	AT	300
REDm	301	AC	AT	AA	AT	GT	AC	CA	AG	AT	300
RedWT	361	TG	CT	TA	AT	GT	AC	CA	AG	AT	420
REDm	361	TG	CT	TA	AT	GT	AC	CA	AG	AT	420
RedWT	421	GAT	TT	CT	TA	AA	AT	TC	AT	AA	480
REDm	421	GAT	TT	CT	TA	AA	AT	TC	AT	AA	480
RedWT	481	GT	AT	TT	AT	TC	CG	TT	AT	TC	540
REDm	481	GT	AT	TT	AT	TC	CG	TT	AT	TC	540
RedWT	541	AA	AG	GT	TT	GT	CC	TT	GT	AA	600
REDm	541	AA	AG	GT	TT	GT	CC	TT	GT	AA	600
RedWT	601	TG	CCA	TA	AG	GT	AA	AT	TA	AG	660
REDm	601	TG	CCA	TA	AG	GT	AA	AT	TA	AG	660
RedWT	661	GAT	CC	CAT	TA	GG	AT	TC	AT	GG	720
REDm	661	GAT	CC	CAT	TA	GG	AT	TC	AT	GG	720
RedWT	721	CA	CA	TC	CT	GG	AC	TT	TC	AG	780
REDm	721	CA	CA	TC	CT	GG	AC	TT	TC	AG	780
RedWT	781	AT	GG	TA	AA	TT	GG	GG	AA	TT	840
REDm	781	AT	GG	TA	AA	TT	GG	GG	AA	TT	840
RedWT	841	T	C	T	AT	TC	CT	CC	AA	TT	900
REDm	841	T	C	T	AT	TC	CT	CC	AA	TT	900
RedWT	901	T	AC	AA	TT	TC	AG	CA	AT	TC	960
REDm	901	T	AC	AA	TT	TC	AG	CA	AT	TC	960
RedWT	961	GC	GA	AA	AG	AT	TC	AA	GG	AT	1020
REDm	961	GC	GA	AA	AG	AT	TC	AA	GG	AT	1020
RedWT	1021	GA	AC	CT	GT	CA	AT	TC	AA	GG	1080
REDm	1021	GA	AC	CT	GT	CA	AT	TC	AA	GG	1080
RedWT	1081	GC	AC	CT	AT	TC	AA	GG	AT	1140	
REDm	1081	GC	AC	CT	AT	TC	AA	GG	AT	1140	
RedWT	1141	GA	AC	AA	AG	GA	AT	TC	AA	GG	1200
REDm	1141	GA	AC	AA	AG	GA	AT	TC	AA	GG	1200
RedWT	1201	AA	CA	TC	CA	GC	AT	TC	GA	GG	1260
REDm	1201	AA	CA	TC	CA	GC	AT	TC	GA	GG	1260
RedWT	1261	CT	GG	TA	AT	TC	AC	GA	AT	TC	1320
REDm	1261	CT	GG	TA	AT	TC	AC	GA	AT	TC	1320
RedWT	1321	AA	TA	TC	AA	GG	CT	TC	GA	GG	1380
REDm	1321	AA	TA	TC	AA	GG	CT	TC	GA	GG	1380
RedWT	1381	AA	TA	TC	AT	TC	GG	AT	TC	GG	1440
REDm	1381	AA	TA	TC	AT	TC	GG	AT	TC	GG	1440
RedWT	1441	GC	GT	GT	AT	TC	GG	CT	TC	GG	1500
REDm	1441	GC	GT	GT	AT	TC	GG	CT	TC	GG	1500
RedWT	1501	GC	GA	GT	AT	TC	AA	GG	AT	TC	1560
REDm	1501	GC	GA	GT	AT	TC	AA	GG	AT	TC	1560
RedWT	1561	CC	AA	GG	CC	AA	AC	GG	AT	TC	1620
REDm	1561	CC	AA	GG	CC	AA	AC	GG	AT	TC	1620
RedWT	1621	J	AG	GG	TA	AT	TC	AA	GG	AT	1641
REDm	1621	J	AG	GG	TA	AT	TC	AA	GG	AT	1641

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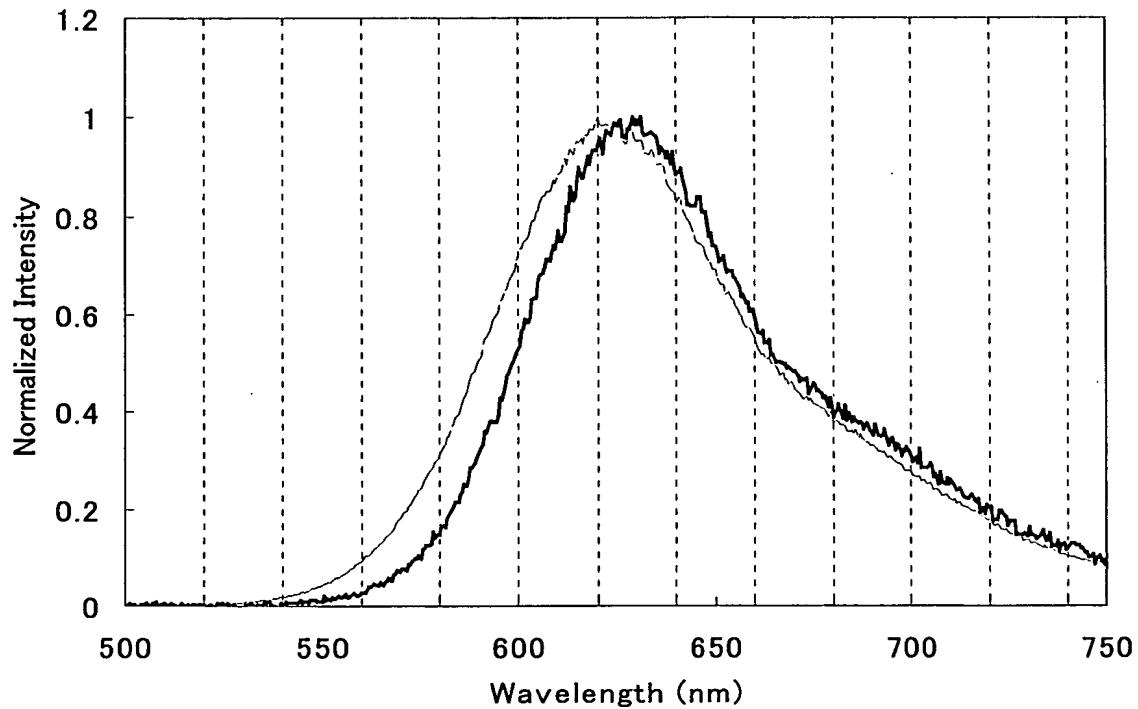
Fig. 14

REDm	1	ATGGAAGAAGAGAACCTTGATGCGATCGGCTGGATCTGGTGTTCCTGGCACA	60
WO2003-016839	1	ATGGAAGAAGAGAACCTTGATGCGATCGGCTGGATCTGGTGTTCCTGGCACA	60
REDm	61	GCCTGGCTCAGCTGTATCAGTCCTGTATAAATACATCACGACGGATATC	120
WO2003-016839	61	GCCTGGCTCAGCTGTATCAGTCCTGTATAAATACATCACGACGGATATC	120
REDm	121	GACGCCCAACCAACGAGGTCTATGCCATATGCCAGATTTGAAACAGTGGCCCTG	180
WO2003-016839	121	GACGCCCAACCAACGAGGTCTATGCCATATGCCAGATTTGAAACCTCCGTG	180
REDm	181	GCCTGTGAGCTGGAGAAGTATGGGCTGGATCACACAACTGGTGGCCATTTGAGCAG	240
WO2003-016839	181	GCCTGTGAGCTGGAGAAGTATGGGCTGGATCACACAACTGGTGGCCATTTGAGCAG	240
REDm	241	AACAAACATCAGCTTTCGGCCCTCTGATCTGCTCCCTTACACGGATTCACATGGCA	300
WO2003-016839	241	AACAAACATCAGCTTTCGGCCCTCTGATCTGCTCCCTTACACGGATTCACATGGCA	300
REDm	301	ACATCAGACGATGTACACGAGAGGGAGATGATGGCCATCTGAACATCTCAAGCCA	360
WO2003-016839	301	ACATCAGACGATGTACACGAGAGGGAGATGATGGCCATCTGAACATCTCAAGCCA	360
REDm	361	TGCTGTATGTTCTGTTCAAGAAATCCTGCCATTCATCTGAAGGTGCAAGAACCTG	420
WO2003-016839	361	TGCTGTATGTTCTGTTCAAGAAATCCTGCCATTCATCTGAAGGTGCAAGAACCTG	420
REDm	421	GACTTTCTTAACTAACTCTTATGACATGAGTATGATCTCATGTACGATATCAAGGGTGGAGTGC	480
WO2003-016839	421	GACTTTCTTAACTAACTCTTATGACATGAGTATGATCTCATGTACGATATCAAGGGTGGAGTGC	480
REDm	481	GTCTTCAGTTTGTCTCCCGTACACGATCACCCGCTTCGAATCAGTGAAGTTCAACCC	540
WO2003-016839	481	GTCTTCAGTTTGTCTCCCGTACACGATCACCCGCTTCGAATCAGTGAAGTTCAACCC	540
REDm	541	AAAGAGTTGACCCCTGGAGAGAACCGCCTGATGACATCCTGGACACAACTGG	600
WO2003-016839	541	AAAGAGTTGACCCCTGGAGAGAACCGCCTGATGACATCCTGGACACAACTGG	600
REDm	601	CTGCCCTAAGGGCTGTGATCAGCCACAGGAGATCACATCAGATTCTGCCACAGCAG	660
WO2003-016839	601	CTGCCCTAAGGGCTGTGATCCTCCACAGATCTCATCAGATTCTGCCACAGCAG	660
REDm	661	GATCCCATCTACGGCACCCTATGCCCGAGATCATCATCTGGCATGCCCTTTC	720
WO2003-016839	661	GATCCCATCTACGGCACCCTATGCCCGAGATCATCATCTGGCATGCCCTTTC	720
REDm	721	CATCACGCCCTGGACTGTTTACGCTCTGGCTTACTTCTGAAAGACCATCTGAAAGATGTC	780
WO2003-016839	721	CATCACGCCCTGGACTGTTTACGCTCTGGCTTACTTCTGAAAGACCATCTGAAAGATGTC	780
REDm	781	ATGGTGAAPAAATTGAGGGCAGTTCTGAAAGACCATCTGAAAGACCATCTGAAAGATGCT	840
WO2003-016839	781	ATGGTGAAPAAATTGAGGGCAGTTCTGAAAGACCATCTGAAAGACCATCTGAAAGATGCT	840
REDm	841	TCTATCTGCTGCTCCCTCTCATATGGTCTATCTGGCAAGAGCCCCTGGTCTATGAA	900
WO2003-016839	841	TCTATCTGCTGCTCCCTCTCATATGGTCTATCTGGCAAGAGCCCCTGGTCTATGAA	900
REDm	901	TACAACTCTGCTCAGCTGACAGACATGCCATGCGCTGGCTCTCTCTGGAGAGACATC	960
WO2003-016839	901	TACAACTCTGCTCAGCTGACAGACATGCCATGCGCTGGCTCTCTCTGGAGAGACATC	960
REDm	961	GGCGAATAGCTGGCCAAGAGACTGAAAGCTCAAGGCTATGGCTATGGCTGACC	1020
WO2003-016839	961	GGCGAATAGCTGGCCAAGAGACTGAAAGCTCAAGGCTATGGCTATGGCTGACC	1020
REDm	1021	GAGACCTGTAGGGCTGTGATCTGACCTGGCCCAACGATCTGAGCTGAAAGAGGGCTATC	1080
WO2003-016839	1021	GAGACCTGTAGGGCTGTGATCTGACCTGGCCCAACGATCTGAGCTGAAAGAGGGCTATC	1080
REDm	1081	GGACCCCTATGCCATATGCTCTGGATGACATCTGGATGACATCAATCCGGTAAAGCCCTG	1140
WO2003-016839	1081	GGACCCCTATGCCATATGCTCTGGATGACATCTGGATGACATCAATCCGGTAAAGCCCTG	1140
REDm	1141	GGACCAAGAGAGAAAGGGAGATCTGCTTCAAGAGCAGATGCTGATGAAGGGTACAC	1200
WO2003-016839	1141	GGACCAAGAGAGAAAGGGAGATCTGCTTCAACTCTGAGATGCTGATGAAGGGTACAC	1200
REDm	1201	ACACATCCAGGGCACAGGGATGCTGGACAGAGCACTGGTGGCTGCACACCTGGCAT	1260
WO2003-016839	1201	ACACATCCAGGGCACAGGGATGCTGGACAGAGCACTGGTGGCTGCACACCTGGCAT	1260
REDm	1261	CTGGGCTATACGACGAGACAGATTCTATGTCCTGGATCGGCTGAAGAGCTGATC	1320
WO2003-016839	1261	CTGGGCTATACGACGAGACAGATTCTATGTCCTGGATCGGCTGAAGAGCTGATC	1320
REDm	1321	AAAGTAAACGGCTAGGTCGCCCTGCTGAGCTGGACACACTGCTCTGGCAGCACCC	1380
WO2003-016839	1321	AAAGTAAACGGCTAGGTCGCCCTGCTGAGCTGGACACACTGCTCTGGCAGCACCC	1380
REDm	1381	AAATCTCTGATGCCGGCGCTATGGCTATGGCTCTGGATCTGGCTGAAAGAGCTGATC	1440
WO2003-016839	1381	AAATCTCTGATGCCGGCGCTATGGCTATGGCTCTGGATCTGGCTGAAAGAGCTGATC	1440
REDm	1441	GCCTGTGTCTGCTGGAGCTGGCAAGACCATGACCGAGAGGAATGCAAGGATATC	1500
WO2003-016839	1441	GCCTGTGTCTGCTGGAGCTGGCAAGACCATGACCGAGAGGAATGCAAGGATATC	1500
REDm	1501	GCAGAGCTGGTACATCACATCACATCTGAGGGGGGGCTGCTTATGATTCATT	1560
WO2003-016839	1501	GCAGAGCTGGTACATCACATCACATCTGAGGGGGGGCTGCTTATGATTCATT	1560
REDm	1561	CCAAAGGCCAACAGGAAACTGATGAGAACAGAATGAGGGCTCTTGGCTGGAG	1620
WO2003-016839	1561	CCAAAGGCCAACAGGAAACTGATGAGAACAGAATGAGGGCTCTTGGCTGGAG	1620
REDm	1621	CAGGCATATCTGAGCTGTAA	1641
WO2003-016839	1621	CAGGCATATCTGAGCTGTAA	1641

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Fig. 15

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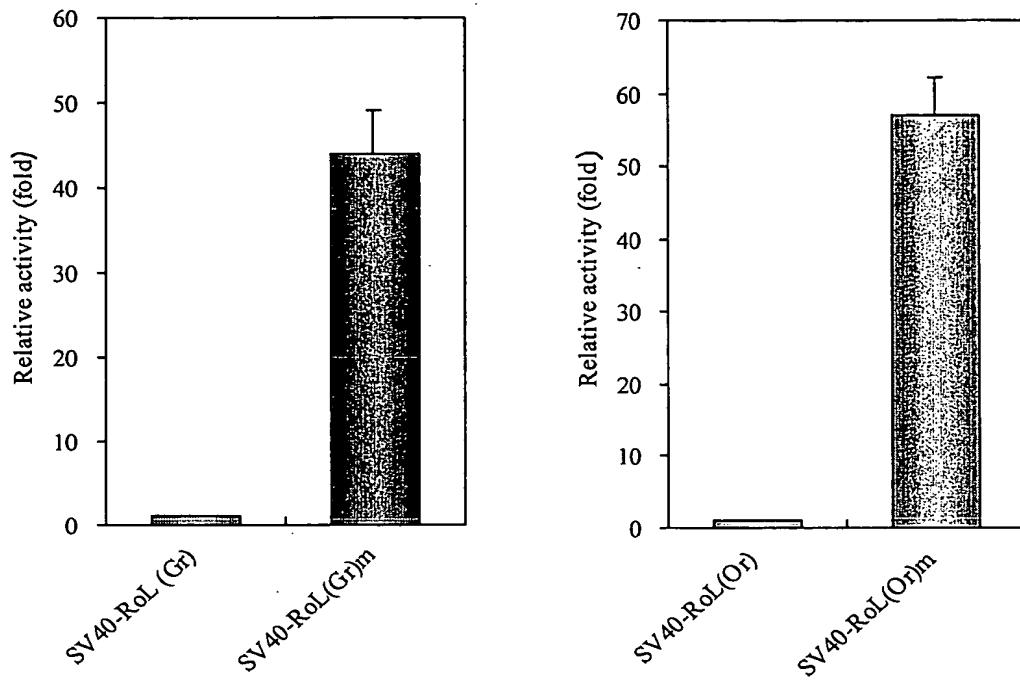
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Fig. 16



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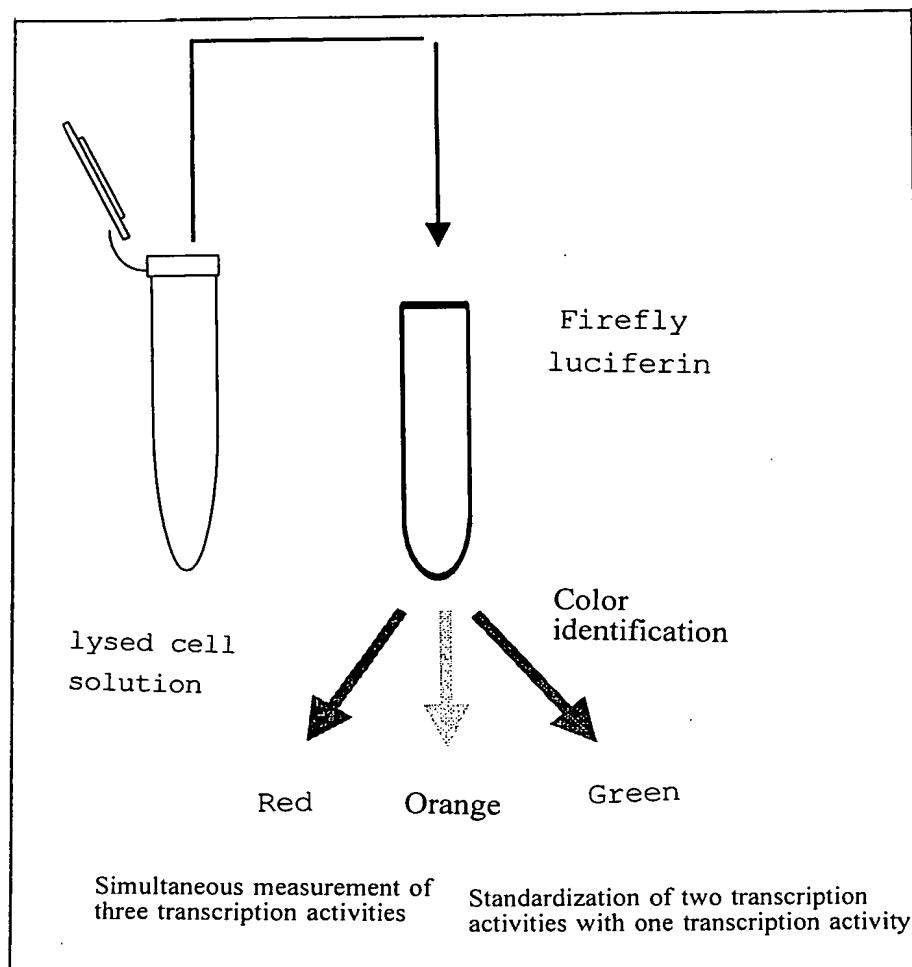
Fig. 17

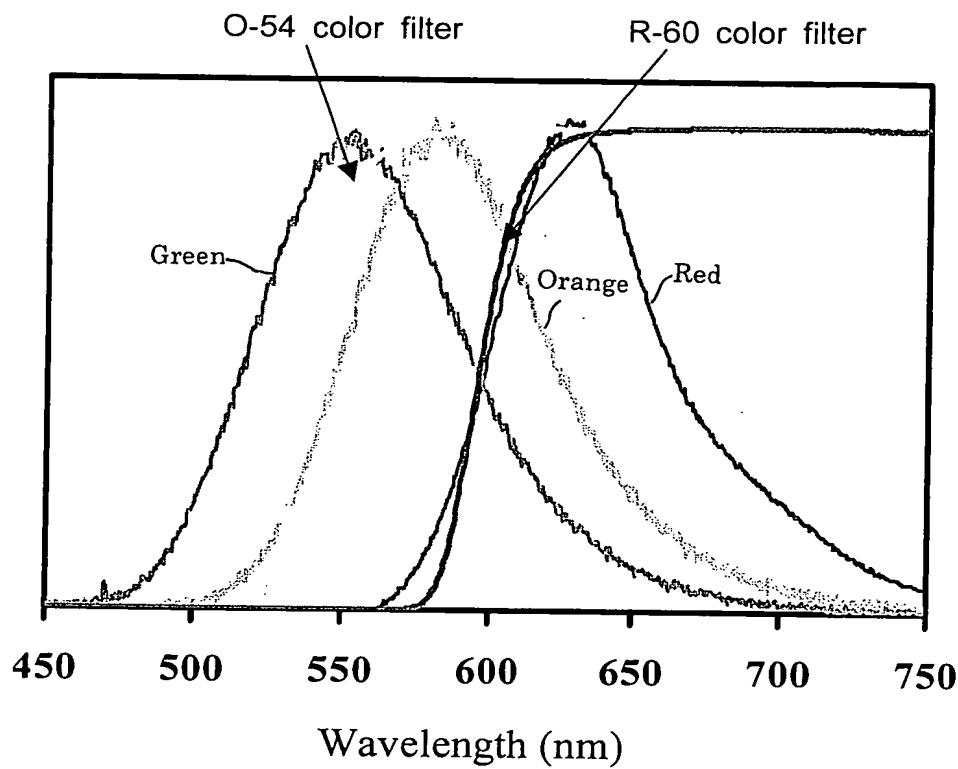
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RoLWT	1	ATGCTTAAGATCATCTTCACGGGCCAAAGCCAGGACCCCTGGACCTGGGACC	60
RoLm	61	SCGGATTAGCTTACGGGCCCTGACCTCTTCTCTCTCTGGGAGGCCCTGATC	120
RoLWT	61	SCGGATTAGCTTACGGGCCCTGACCTCTTCTCTCTGGGAGGCCCTGATC	120
RoLm	121	SACGCCACACCGGAGGAGCTCTTACCTACGGGAGGAGCTTACAGCTGTAATG	180
RoLWT	121	SACGCCACACCGGAGGAGCTCTTACCTACGGGAGGAGCTTACAGCTGTAATG	180
RoLm	181	GCAGATGCTACGAACTAAGCCCTGGGAAACAGCGCTATCTGTGAGCGAG	240
RoLWT	181	GCAGATGCTACGAACTAAGCCCTGGGAAACAGCGCTATCTGTGAGCGAG	240
RoLm	241	AAAGCACCCTCTTCTTACCCCGTATCTCCGGCTGTATATGGGGGTGATACGCC	300
RoLWT	241	AAAGCACCCTCTTCTTACCCCGTATCTCCGGCTGTATATGGGGGTGATACGCC	300
RoLm	301	ACCGTAAAGATGTTACCGAGGGAGCTCTGGACCCCTGGATATCTTACCGC	360
RoLWT	301	ACCGTAAAGATGTTACCGAGGGAGCTCTGGACCCCTGGATATCTTACCGC	360
RoLm	361	GAATCTGTTCTGCTCAAGAACCCATTAAGAACATGATGGCCCTGAAAGGGAAACGTG	420
RoLWT	361	GAATCTGTTCTGCTCAAGAACCCATTAAGAACATGATGGCCCTGAAAGGGAAACGTG	420
RoLm	421	AAATTCTTAAAGGTGTTCTGGCTGGAAAGGAAATATGGGGAGGCCAGTGTG	480
RoLWT	421	AAATTCTTAAAGGTGTTCTGGCTGGAAAGGAAATATGGGGAGGCCAGTGTG	480
RoLm	481	CTTAGCAACTTATGGCCGGTACTCGAACTCCACCGTGGACGTAGAACCTTACCGA	540
RoLWT	481	CTTAGCAACTTATGGCCGGTACTCGAACTCCACCGTGGACGTAGAACCTTACCGA	540
RoLm	541	ACGACTTGAACGCTTACGGGAAACAGCTGGCCCTATATGTCCTCTGGGACACC	600
RoLWT	541	ACGACTTGAACGCTTACGGGAAACAGCTGGCCCTATATGTCCTCTGGGACACC	600
RoLm	601	CTGCCAAAGGGCTCTGTTACCCACAACTACCGTGGCGTSEGGCTTCGTCACTGCAAG	660
RoLWT	601	CTGCCAAAGGGCTCTGTTACCCACAACTACCGTGGCGTSEGGCTTCGTCACTGCAAG	660
RoLm	661	GACCCCTTGGTGGCACAGAACATCCCTCCACCTCCATCTGGCTATCGTCTCC	720
RoLWT	661	GACCCCTTGGTGGCACAGAACATCCCTCCACCTCCATCTGGCTATCGTCTCC	720
RoLm	721	CAACATGCCCTTGGAAATGTTTACAACCCCTGTCCTACTTATCTGGCTTCTAGAGTGGT	780
RoLWT	721	CAACATGCCCTTGGAAATGTTTACAACCTGTCCTATTTATAGGGCTTCTAGAGTGGT	780
RoLm	781	CTCTGAAGAGATTGCGAGGAGAAAGTTTTCCTGAGCACCATCGAGAAAGTACAGAACTCCA	840
RoLWT	781	CTCTGAAGAGATTGCGAGGAGAAAGTTTTCCTGAGCACCATCGAGAAAGTACAGAACTCCA	840
RoLm	841	ACATATCGTCTGGCCCTGGCTATGGTCTTCTGGCTAAGAGCCCCCTGGGACCGAG	900
RoLWT	841	ACATATCGTCTGGCCCTGGCTATGGTCTTCTGGCTAAGAGCCCCCTGGGACCGAG	900
RoLm	901	TACGACCTGTCCAGCATAGAGAGCTGGACCCGGGGCGCTCTGGGACCGAGTT	960
RoLWT	901	TACGACCTGTCCAGCATAGAGAGCTGGACCCGGGGCGCTCTGGGACCGAGTT	960
RoLm	961	CGGTGGCCGTTGGCAAGCGTGAAGATGGCGGATCTCTGGGGCTACGGGCTGGACC	1020
RoLWT	961	CGGTGGCCGTTGGCAAGCGTGAAGATGGCGGATCTCTGGGGCTACGGGCTGGACC	1020
RoLm	1021	GGAGACCTGCGGCGCTGCGTACCCCGTACGGACGTTAGACGGCTCCACCGG	1080
RoLWT	1021	GGAGACCTGCGGCGCTGCGTACCCCGTACGGACGTTAGACGGCTCCACCGG	1080
RoLm	1081	AGGGTAGGCCCTACGGCTACGGCTAGATCTGGTACCTGACCCACCGGAAATCTGGGAA	1140
RoLWT	1081	AGGGTAGGCCCTACGGCTACGGCTAGATCTGGTACCTGACCCACCGGAAATCTGGGAA	1140
RoLm	1141	CCAAATAGAGGAGGAGGAGCTTGTTTAAAGCTGAGATCATATGAAAGGGCTATTCAAC	1200
RoLWT	1141	CCAAATAGAGGAGGAGCTTGTTTAAAGCTGAGATCATATGAAAGGGCTATTCAAC	1200
RoLm	1201	AAATACGACCGACGACGACGACGACGACGACGACGACGACGACGACGACGACGACG	1260
RoLWT	1201	AAATACGACCGACGACGACGACGACGACGACGACGACGACGACGACGACGACGACG	1260
RoLm	1261	GGATATGACGACGACGATGGCTATTTCTTCGTTGTCGACCGCTGAAAGGACCTGATCAAG	1320
RoLWT	1261	GGATATGACGACGACGATGGCTATTTCTTCGTTGTCGACCGCTGAAAGGACCTGATCAAG	1320
RoLm	1321	TACAAGGGTACCAAGTCGCGGCCGCGTACGGCTGGAGGTGGCTGCTGCTGCTGCTGCTG	1380
RoLWT	1321	TACAAGGGTACCAAGTCGCGGCCGCGTACGGCTGGAGGTGGCTGCTGCTGCTGCTG	1380
RoLm	1381	ATCAAAGATGCCGGCTGGCGGGCTGGCGGCTGGCGACGGACCTGGCTGGCGGGCG	1440
RoLWT	1381	ATCAAAGATGCCGGCTGGCGGGCTGGCGGCTGGCGACGGACCTGGCTGGCGGGCG	1440
RoLm	1441	TGATATGTTCTCAAGAAAGTACGATCTGACGACGATATGACGATATGACGATATGCC	1500
RoLWT	1441	TGATATGTTCTCAAGAAAGTACGATCTGACGACGATATGACGATATGACGATATGCC	1500
RoLm	1501	GAGCGAGTGTCTCCACGACGACGACGACGACGACGACGACGACGACGACGACGACG	1560
RoLWT	1501	GAGCGAGTGTCTCCACGACGACGACGACGACGACGACGACGACGACGACGACGACG	1560
RoLm	1561	AAAGGGCGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGG	1620
RoLWT	1561	AAAGGGCGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGGCTGG	1620
RoLm	1621	TGCTTATGTTAA	1632
RoLWT	1621	TGCTTATGTTAA	1632

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Fig. 18

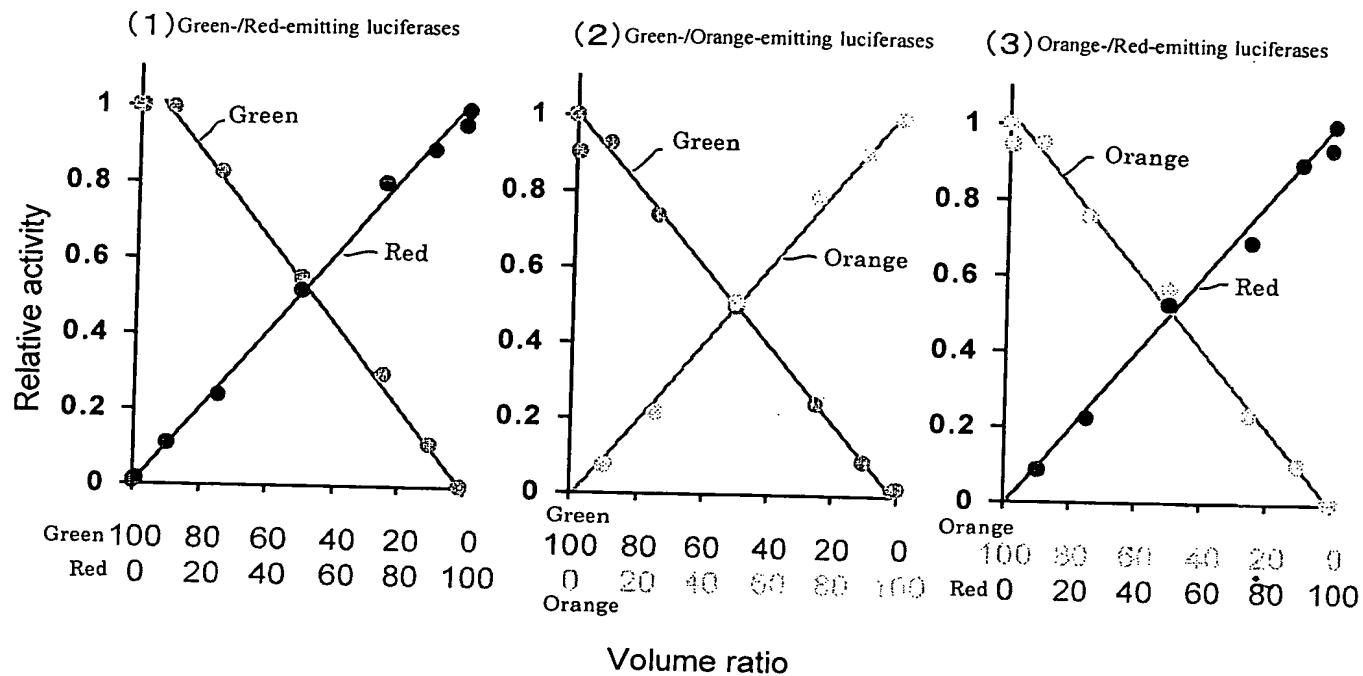
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Fig. 19



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Fig. 20

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Fig. 21



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Fig. 22